REMARKS

Claims 1-2 and 8-12 are pending in this application.

Applicant has amended Claim 1, as filed. Applicant respectfully submits that this application is now in condition for allowance.

CLAIM OBJECTIONS

Applicant notes that the Examiner rejected Claims 1-2 and 8-12 under 35 U.S.C. §112, first paragraph. Particularly, the Examiner indicates that, "The specification has not provided enablement for a method of screening for an agent that modulates bone mineralization in any bone tissue said method comprises contacting the any cell containing a Nell-1 gene with a test agent..." (Page 3) The Applicant disagrees with the Examiner's characterization of the pending claims and the art cited. However, to advance prosecution in this case, the Applicant has amended Claim 1, and added Claim 50.

As Examiner admits Applicants have demonstrated that Nell-1 enhances mineralization in osteoblastic cells, irrespective of the hypothesized mechanism of action. (Page 3, Line 20). However, the Examiner further states that "Nell-1 has no function in the vast majority of bone mineralization (Page 5)...there is no evidence for a role of Nell-1 in bone mineralization in general in the fetus (Page 6)." However, the Applicant's respectfully submit that the specification and references cited by the Examiner do not support such a conclusion.

One embodiment of the specification specifically demonstrates endogenous Nell expression in osteoprogenitor cells, mesenchymal cells and osteoblastic cells, as well as induced expression of Nell-1 in MC3T3 cells and rat fetal calvarial primary cell cultures (Specification, page 41). Specifically, over expression of Nell-1 in the cell cultures lead to enhanced mineralization.

Further, Ting (1999) describes Nell-1 localization primarily in the calvarial osteoprogenitor cells (i.e. mesenchymal cells and osteoblasts at the osteogenic font; intramembraneous bone). (Noted at Office Action at Page 5). However, Ting also discloses *nel* in chick limb development (endochondral bone)(Page 86, col. 2). Finally, Zhang describes Nell-1 expression in "bone forming areas of sutures and the calvarium

and ossifying membranous bone in the mandible (Page 869, col. 1). Therefore, the specification and references cite indicate Nell-1's expression in a variety of osteogenic tissues, and correlates to mineralization in osteogenic cells.

Further, Applicant notes that the specification is enabling for the claims presented. Given the teachings of the specification, the amount of experimentation required by one skilled in the art to determine if test agents effect mineralization in osteogenic cells would be routine (Specification, Page 4). The presence of inoperable embodiments within the scope of a claim does not necessarily render it non-enabled (MPEP 2164.08(b)). One skilled in the art could readily determine whether embodiments of the invention were operative by verifying the effect of a test agent on osteogenic cells' ability to induce mineralization, as described (Specification, page 42).

Applicant's note that the art cited by the Examiner is not prior art to the present invention, and understand that the Examiner has cited this art to reflect the level and knowledge of skill in the art circa the time of the invention.

CONCLUSION

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 501946 and please credit any excess fees to such deposit account.

Respectfully submitted,
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